Revista da Sociedade Brasileira de Medicina Tropical
27(1):39-42, jan-mar, 1994

RELATO DE CASO

LEPTOSPIROSIS PATIENT WITH AIDS THE FIRST CASE REPORTED

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A case of renal icterohaemorrhagic leptospirosis involving a patient with acquired immunodeficiency syndrome (AIDS) is reported. Despite the low levels of CD_4^+ T lymphocytes, the clinical course of leptospirosis was similar to that observed in non-immunodepressed patients, and no worsening of AIDS occurred due to the infection by the spirochete. Serologic conversion was observed in the microscopic agglutination test, with maximum titer of 1:3,200. The patient had positive urine cultures for Leptospira interrogans *for two months, whereas blood cultures were negative.*

Key-words: Leptospirosis. Case report. Leptospira interrogans. *AIDS.*

The acquired immunodeficiency syndrome (AIDS) is a pandemic disease of growing importance, with 29,644 cases reported in Brazil by August 1992[5]. The city of Rio de Janeiro is the second in the country in number of patients, with 3,593 cases notified by the same date and with an incidence of 64.8 per 100,000 inhabitants[7]. In turn, leptospirosis is endemic, with epidemic outbreaks occurring during the summer months due to the more intensive rainfall. A total of 863 cases have been notified from 1987 to 1991, 55.5% of which caused by an epidemic in the summer of 1988[8].

We report a case of leptospirosis (icterohemorrhagic form) involving a patient with Group IV C_2 AIDS.

CASE REPORT

A mulatto male has been followed up at the Virology Outpatient Clinic of the Evandro Chagas Hospital (ECH) since 1987 because of AIDS and lymphatic tuberculosis. HIV infection was confirmed by the presence of specific serum antibodies detected by ELISA and by indirect immunofluorescence, and tuberculosis was determined by the detection of alcohol-acid-resistant bacilli in the histopathological examination of a lymphnode biopsy.

Specific triple treatment of tuberculosis consisted of rifampicin and isoniazid for six months in combination with pyrazinamide during the first two months. Isoniazid was also used for suppressive treatment. Typing of lymphocyte subpopulations by flow cytometry at the time of treatment indicated 255 CD_4^+ T lymphocytes and 1018 CD_8^+ lymphocytes/mm^3. The CD_4^+/CD_8^+ ratio was 0.25.

The patient gave up treatment in December 1988, and returned to our Service in August 1991, with oral candidiasis and a 14kg weight loss, with no fever or other manifestations of reactivation of tuberculosis. He had not been taking any medication since the time when he stopped treatment. Nystatin was introduced for the treatment of candidiasis, together with sulfamethoxazole-trimetoprim for primary prophylaxis of pulmonary pneumocystosis, 500mg/day zidovudine, and 7,200,000 IU penicilin G benzatine as total dose for the treatment of late secondary syphilis, because of the detection of positive VDRL test with 1/64 titer and normal cerebrospinal fluid. The patient has been complying with the above treatment and has been followed up at the Service since he reappeared in August 1991.

In August 1992, he came to the ECH 13 days after falling in a ditch in the slum where he lived presenting high fever, myalgia predominating in the lower limbs, vomiting and headache lasting 6

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Recebido para publicação em 08/10/93.

days. He had been presenting jaundice, epistaxis and reduced urinary output for 2 days. Arterial pressure, 80x60mm Hg; heart rate, 80 beats per minute; respiratory rate, 20 inspirations per minute; axillary temperature, 36.5°C. Neurologic, pulmonary and cardiac examination were normal. The abdomen was painful upon superficial and deep palpation, with spleen palpable 1cm from the left coastal margin. No skin lesions. Emergency biochemical blood tests revealed 184mg/dl urea, 5.3mg/dl creatinine, 140mEq/l sodium, and 4.3mEq/l potassium. Blood counts revealed 33% hematocrit, 3,000,000 red cells/mm^3, 10.7g/% hemoglobin, 2,500 leukocytes/mm^3 (0/1/0/0/2/82/14/1), and 32,000 platelets/mm^3. Prothrombin activity was 60%, and a chest X-ray was normal.

With a diagnostic hypothesis of leptospirosis, later confirmed by the microscopic agglutination* test and by the isolation of *Leptospira interrogans* in urine cultured in Ellinghausen medium (EMJH)[4] (Table 1), water and electrolyte repletion was started and dopamine, diuretics and a platelet concentrate were introduced. A hematological evaluation was made 28 days after the onset of symptoms. The patient presented a low number of lymphocytes (550/mm^3) from which a small fraction reacted with monoclonal antibodies specific for CD_4^+ T lymphocytes (13/mm^3) and CD_8^+ T lymphocytes (68/mm^3). The CD_4^+/CD_8^+ ratio was also reduced (0.19) in relation to the first examination.

The patient's course was satisfactory, with regression of renal insufficiency on the 7th day of hospitalization. However, he continued to have daily fever, with no relation to a specific time of day and not exceeding 38.5°C. No chills were present.

To clarify the origin of fever, blood, urine, sputum and bone marrow cultures were performed, and lymphnode, liver and bone marrow biopsies were taken. Since the cultures were negative and the biopsies inconclusive, empirical treatment of tuberculosis with rifampicin, isoniazid and pyrazinamide was introduced and discontinued after one month due to the absence of a response and to the presence of signs of liver toxicity. The patient was discharged on October 16, 1992 in improved general condition and with decreased fever intensity.

On the occasion of the first reevaluation at the outpatient clinic 12 days after discharge from the hospital, the results of the *Leptospira sp.* cultures were available. Blood cultures in EMJH medium were negative, but urine culture revealed the growth of *Leptospira interrogans* up to the 60th day of disease. The evolution of the microscopic agglutination titers and the results of the cultures are presented in Table 1. In view of these results, tetracycline was administered at a daily dose of 2g for 21 days, since serology continued to be positive also for syphilis.

When the patient was evaluated again 13 days later he was asymptomatic and had gained 7kg. Another urine culture for *Leptospira sp.* gave negative results.

In January, 1993, signs of dementia associated with progressive cachexia appeared. The patient was admitted to the hospital twice, with severe

Table 1 - Results of serum microscopic agglutination test (1:), and blood and urine culture to Leptospira sp in AIDS patient.

Day of ilness	Serovar				Culture	
	1	2	3	4	blood	urine
6th	0	0	0	0	ND	ND
10th	3,200	0	0	0	-	+
60th	1,600	800	400	400	-	+
70th	1,600	800	400	100	-	-
100th	400	200	0	0	-	-

ND - not done; Serovar: 1 = *icterohaemorrhagiae*; 2 = *copenhageni*; 3 = *sentot*; 4 = *patoc*

* Note: the serovars used in the microagglutination test were: *icterohaemorrhagiae, copenhageni, javanica, canicola, castellonis, pyrogenis, cynopteri, autumnalis, sentot, djasiman, australis, pomona, grippotyphosa, hebdomadis, wolffi, sejroe, saxkoebing, bataviae, tarassovi, panama, andamana, celledoni, shermani.*

weight loss, fever, confusion, and developed septicemia and acute renal insufficiency, dying one month later. Blood and urine cultures taken one day before death were negative to *Leptospira sp.* Microscopic agglutination test gave a titer of 1:100 to serovar *Leptospira icterohaemorrhagiae.*

At the autopsy, the cause of death was bronchopneumonia due to Gram-negative cocci. HIV-related subacute encephalitis and muscular atrophy were observed. Finally, cachexia, molluscum contagiosum, dermatophytosis, gastric erosions, acute pancreatitis with steatonecrosis, multiple septic pulmonary infarct and herpesvirus colitis were also present. Leptospirosis lesions were not observed and silver stain did not reveal spirochaetal forms.

DISCUSSION

Human immunodeficiency virus (HIV) leads to dysfunction of the immunologic system, with the consequent occurrence of infections which depend on a faulty cell immune response. Thus, infections caused by opportunistic agents such as *Pneumocystis carinii*, *Cytomegalovirus* and *Cryptosporidium sp.* start to be observed[3].

The occurrence of leptospirosis, in turn, depends on exposure of susceptible individuals to water or soil contaminated with infected urine containing *Leptospira interrogans*. Laborers, animal breeders, miners, urban sanitation workers, butchers, and veterinarians represent the occupational group at risk to contract leptospirosis in areas where the disease is endemic[4]. In Brazil, however, individuals living in dwellings with inadequate basic sanitation, such as city slums, are more exposed to the infection[6].

The case described here was the first report of association of leptospirosis with acquired immunodeficiency syndrome. Two cases of leptospirosis in HIV-infected patients have been reported[9]. The authors reported that the coexistence of the two entities did not interfere with the evolution of either. Similarly, in the present study no change in the behavior of AIDS or of leptospirosis was observed.

Yamashiro-Kanashiro et al[10] demonstrated that patients with leptospirosis present an important reduction of the cell immune response as determined by functional tests and by evaluation of mononuclear cell subpopulations, with depletion of CD_4^+ T lymphocytes and total (CD_3^+) T lymphocytes. The present patient had very low total lymphocyte levels as well as very low levels of the CD_4^+ and CD_8^+ T subpopulations which, however, did not significantly interfere with the course of leptospirosis. This suggests that the mechanism of leptospire elimination is not exclusively related to helper T cells. However, the maximum agglutinating antibody levels were lower than those detected in most of the cases observed in Brazil[2]. This finding may perhaps be explained by the immunodepression of the patient caused by AIDS.

We should point out the persistence of a positive urine culture for *Leptospira interrogans* over a long period of time, a fact observed only in a small percentage of patients[1].

Finally, the absence of any evidence of persistent leptospirosis at autopsy must be emphasized.

RESUMO

Os autores relatam um caso de forma ícterohemorrágica de leptospirose ocorrida em paciente com síndrome de imunodeficiência adquirida (SIDA). A evolução clínica da leptospirose se deu de modo semelhante ao observado em pacientes sem imunodepressão, apesar dos níveis muito baixos de linfócitos T CD_4^+. Tampouco houve agravamento da SIDA em decorrência da infecção pelo espiroqueta. Observou-se conversão sorológica na prova de aglutinação microscópica com títulos máximos de 1:3.200. O paciente permaneceu por dois meses com urinocultura positiva para Leptospira interrogans, *sendo as hemoculturas negativas.*

Palavras-chaves: Leptospirose. Relato de caso. Leptospira interrogans. SIDA.

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